Afdeling

Afd. Medische Microbiologie & Infectieziekten

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Docket No.00D-0109
Dockets Management Branch
Division of Management Systems and Policy
Office of Human Resources and Management Services
Food and Drug Administration
5630 Fishers Lane, Room 1061, (HFA-305),
Rockville , MD 20852
USA

Re: comment on Draft Guidance on Review criteria for assesment of antimicrobial susceptibility devices

Dear Sir/Mrs.,

With great interest I have read the draft guidance on review criteria for assesment of antimicrobial susceptibility devices, that was released for public comment on March 8, 2000. As head of the department of Medical Microbiology and Infectious Diseases of the Erasmus University Medical Center in Rotterdam we have been involved in assesments of such devices in the past and will continue to be involved in the near future. We are currently evaluating the Vitek II machine of the bioMerieux company.

The draft guidance will be of much help in our efforts to evaluate the quality and usefullness of such devices, and we congratulate you with the quality of the draft. There is one point of concern, however, that I would like to share with you. I refer to the article 4 Performance Criteria on page 6 and 7 , the article 12.1 that specifies acceptable perfomance and the tables 5 and 6 that specify these variables as a function of the number of strains tested. As I read this part of the guidance these criteria regarding the percenta agreements and errors are not meant to be new, i.e. they were at the same levels as stated in the current 1991 guidance, but have now been further defined in statistical terms. Thus >90% agreement is part of the 1991 guidance but was not further defined statistically, i.e. the guidance could be interpreted such that during testing the *observed* agreements were >90%. The new draft-guidance, however, aims to make sure that the percent agreements are *truly* >90%, which can be substantiated by requiring a statistical estimate of the true percent agreement by calculating confidence intervals around observed percentages of agreement and setting the lower limit of these confidence intervals to be >90%. Although I fully agree with the use of confidence intervals around observed rates by way of evaluating a susceptibility device, this futher definition of the criteria will in practice require the observed percentages of agreements to be significantly higher than 90%, especially when relatively small numbers of (resistant) strains are tested or available for testing. Thus the draft-guidance

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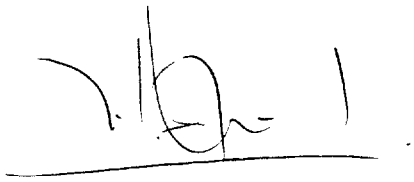
criteria are significantly more demanding than the previous/current one, which may not have been the intent of the authors, and may unduly hamper the introduction of new susceptibility devices. Devices currently on the market have not been subjected to these new criteria since the rates of agreement and errors observed during their evaluation may well have confidence intervals, calculated a posteriori, that go beyond the new limits.

The question then arises what the minimum levels of agreement or maximum rates of errors and the confidence limits around observed percentages of agreements/erros should be. These should be redefined in the light of a) the levels of agreeements and error rates that can be observed when one would simultaneously use two different *reference* methods and compare results between those two methods using one as the reference method and the other as the method under evaluation (and vice versa, so that one can estimate the *maximum* levels of quality that can currently be obtained in susceptibility testing), and b) the minimum levels of agreement and maximum levels of errors that are clinically acceptable, relevant or desirable. Once these levels have been defined, however, I do feel that the use of confidence intervals is crucial in estimating the true quality of these machines.

Thank you for your attention,

Sincerely Yours,



prof. Henri A. Verbrugh, MD PhD

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30.05.00

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